

CLAIMS

1. An Ig fraction, characterized in that it reacts with at least one component selected from IgMs, IgG F(ab')₂s and the hapten DNP, with a level of enrichment of greater than 20 compared to the activity of the initial polyvalent Igs, and in that it does not react with the tetanus toxoid or the HBS antigen, with a level of enrichment of less than 5 compared to the activity of the initial polyvalent Igs.
2. The Ig fraction as claimed in claim 1, characterized in that it consists of an IgG or IgM fraction.
3. The fraction as claimed in either of claims 1 and 2, characterized in that it reacts with a component selected from IgMs, IgG F(ab')₂s and the hapten DNP, with a level of enrichment of greater than 40 compared to the activity of the initial polyvalent Igs.
4. The fraction as claimed in one of claims 1 to 3, characterized in that it reacts with at least one of the autoantigens selected from myosin, actin, tubulin and myelin basic protein (MBP), with a level of enrichment of greater than 10 compared to the activity of the initial polyvalent Igs.
5. The fraction as claimed in claim 4, characterized in that it reacts with at least one of the autoantigens selected from myosin, actin, tubulin and MBP, with a level of enrichment of greater than 20 compared to the activity of the initial polyvalent Igs.
6. The fraction as claimed in one of claims 1 to 5,

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characterized in that it reacts with myosin, actin, tubulin and MBP.

- 5 7. The fraction as claimed in one of claims 1 to 6, characterized in that it reacts with a component selected from IgMs, IgG F(ab')₂s and the hapten DNP, with a level of enrichment of greater than 40 compared to the activity of the initial polyvalent Igs, and with myosin, actin, tubulin and MBP, with a mean level of enrichment of greater than 20 compared to the activity of the initial polyvalent Igs.
- 10 8. The fraction as claimed in one of claims 1 to 7, characterized in that it reacts with IgMs or IgG F(ab')₂s.
- 15 9. The fraction as claimed in one of claims 1 to 7, characterized in that it reacts with the hapten DNP and in that it does not react with IgMs and IgG F(ab')₂s.
- 20 10. A method for preparing Ig fractions, characterized in that it comprises the following steps:
- 25 a) preparing an insoluble support onto which is grafted a component selected from polyvalent IgGs, polyvalent IgMs and DNP-lysin,
- 30 b) adsorbing polyvalent Igs onto the support obtained in step a),
- 35 c) eluting the Igs retained on the portion of immunoglobulins bound to the support, so as to collect the fraction connected through IgG-IgG or IgM-IgG idiotypic interactions, or eluting the fraction which interacts with DNP,
- d) selecting the fractions having reactivity with respect to IgMs, IgG F(ab')₂s or the hapten DNP, little or no reactivity with respect to non-self antigens and/or polyreactivity with respect to given autoantigens,

e) selecting the fractions having activity which inhibits the proliferation of lymphocytes in mixed culture, preferably with an effectiveness 10 to 50 times greater than TEGELINE®.

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11. The method as claimed in claim 10, characterized in that the Igs absorbed consist of IgGs or IgMs.

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12. The method as claimed in either of claims 10 and 11, characterized in that the Ig fractions are prepared from polyvalent Igs or any other intermediate fraction obtained during the method for producing IVIGs for therapeutic use.

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13. The method as claimed in claim 12, characterized in that the polyvalent Igs used to prepare the fractions consist of IgGs or IgMs.

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14. The method as claimed in one of claims 10 to 13, characterized in that step d) comprises measuring the level of enrichment of antibodies reactive against IgMs, IgG F(ab')₂s or the hapten DNP used for the purification.

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15. The method as claimed in one of claims 10 to 14, characterized in that step d) comprises measuring the reactivity for the tetanus toxoid and the HBs antigen, taking the level of enrichment as a control value.

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16. The method as claimed in one of claims 10 to 15, characterized in that step d) comprises an ELISA assay carried out on a panel of autoantigens selected in particular from actin, myosin, MBP and tubulin.

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17. The method as claimed in one of claims 10 to 16, characterized in that step d) comprises a competition assay in order to control the

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neutralizing activity of the fractions with respect to autoantibodies originating from serum of patients suffering from autoimmune diseases.

- 5 18. The method as claimed in one of claims 10 to 17, characterized in that step d) comprises an assay of inhibition of the mixed lymphocyte reaction with human cells in order to control the reactivity of the purified Igs.
- 10 19. The method as claimed in one of claims 10 to 18, characterized in that step a) consists in grafting polyvalent IgGs, polyvalent IgMs or DNP-Lysine onto an insoluble support, in particular onto a
- 15 Sepharose®, Trisacryl®, Affiprep® or Affigel® gel, or gels activated with the groups CNBr, NHS or C₅H₈O₂ (glutaraldehyde).
- 20 20. The method as claimed in one of claims 10 to 19, characterized in that the Igs deposited onto the solid support obtained in step a) are adsorbed either in the form of polyvalent IgGs lyophilized and redissolved or in liquid form, or in the form of intermediate fractions obtained during a method
- 25 for producing polyvalent IgGs, in 20 mM phosphate buffer containing NaCl, the concentration of which may range from 0 M to 3 M.
- 30 21. The method as claimed in one of claims 10 to 20, characterized in that the Igs retained in step b) are eluted with a buffer containing ions which dissociate Ag-Ab or Ag-DNP binding, selected in particular from chaotropes such as glycine-HCl or sodium iodide (NaI), under conditions which vary
- 35 the pH, preferably between 2.8 and 4.0, and/or the molarity of the buffer.
22. The method as claimed in one of claims 10 to 21, characterized in that the absorption is carried

out under temperature conditions ranging from 4° to 40°C and in PBS.

23. The method as claimed in one of claims 10 to 22, characterized in that, in step d), fractions as claimed in one of claims 1 to 9 are selected.

24. A method for the industrial production of fractions having reactivity with respect to a component selected from IgMs, IgG F(ab')₂s and the hapten DNP, little or no reactivity with respect to non-self antigens and polyreactivity with respect to given autoantigens, characterized in that steps a), b) and c) of claim 10 are carried out, respecting or adjusting the parameters used in preparing the fractions of interest selected beforehand.

25. A fraction which can be obtained using a method as claimed in one of claims 10 to 24.

26. The use of an Ig fraction as claimed in one of claims 1 to 9 and 25, for preparing a medicinal product.

27. The use as claimed in claim 26, for preparing a medicinal product intended for the treatment of autoimmune diseases, or GVH and/or of graft rejection after transplantation.

28. The use as claimed in claim 26, for preparing a medicinal product intended for the treatment of Kawasaki disease, for the treatment of Birdshot retinochoroiditis, optionally in combination with corticotherapy, and/or for the treatment of certain cytopenias and/or of hemophilias with inhibitors (anti-factor VIII autoantibodies), and/or for preventing and/or impeding immune rejection of cell and/or organ transplants and the

development of GVH after transplantation of
allogenic hematopoietic cells.

- 5 29. The use as claimed in claim 26, for preparing a
medicinal product intended for the treatment of
neurological diseases, in particular adult
Guillain-Barré syndrome, chronic demyelinating
inflammatory polyneuropathies, dermatomyositis,
myasthenia and/or multiple sclerosis.

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